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ORIGINAL PAPER

Computed tomography for planning and postoperative imaging of transvenous mitral annuloplasty: first experience in an animal model

Simon H. Sündermann · Sonja Gordic · Robert Manka · Nikola Cesarovic · Volkmar Falk · Francesco Maisano · Hatem Alkadhi

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Abstract To investigate the use of computed tomography (CT) to measure the mitral valve annulus size before implantation of a percutaneous mitral valve annuloplasty device in an animal trial. Seven domestic pigs underwent CT before and after implantation of a Cardioband^{TM} (a percutaneously implantable mitral valve annuloplasty device) with a second-generation 128-section dual-source CT machine. Implantation of the Cardioband^{TM} was performed in a standard fashion according to a protocol. Animals were sacrificed afterwards and the hearts explanted. The Cardioband^{TM} was found to be adequately implanted in all animals, with no anchor dehiscence and no damage of the circumflex artery (CX) or the coronary sinus (CS). The correct length of the band as chosen according to the length of the posterior mitral annulus measured in CT before implantation was confirmed in gross examination in all animals. The device did not result in a metal artifact-related degradation of image quality. The closest distance from the closest anchor to the CX was 2.1 ± 0.7 mm in diastole and 1.6 ± 0.5 mm systole. Mitral annulus distance to the CS was 6.4 ± 1.3 mm in diastole and 7.7 ± 1.1 mm in systole. CT visualization and measurement of the mitral valve annulus dimensions is feasible and can become the imaging method of choice for procedure planning of Cardioband^{TM} implantations or other transcatheter mitral annuloplasty devices.

Keywords Computed tomography · Mitral annuloplasty · Heart · Mitral annulus

Abbreviations

CT	Computed tomography
CX	Circumflex artery
ECG	Electrocardiogram
FoV	Field of view
ICE	Intracardiac echocardiography
IVC	Inferior vena cava
MR	Mitral valve regurgitation
MVR	Mitral valve repair
SAFIRE	Sinogram-affirmed iterative reconstruction
TAVI	Transcatheter aortic valve implantation
TSchG	Swiss Animal Protection Law
TSchV	Swiss Animal Protection Act

Introduction

Mitral valve repair (MVR) has become the gold standard therapy for severe mitral valve regurgitation (MR) with excellent results [1, 2]. However, due to age, comorbidities, and poor left ventricular function up to 50 % of symptomatic patients with severe MR are not referred to surgery [3].

S. H. Sündermann · V. Falk · F. Maisano
Division of Cardiovascular Surgery, University Hospital Zurich, Zurich, Switzerland

S. Gordic · R. Manka · H. Alkadhi (✉)
Institute of Diagnostic and Interventional Radiology, University Hospital Zurich, Zurich, Switzerland
e-mail: hatem.alkadhi@usz.ch

R. Manka
Clinic of Cardiology, University Hospital Zurich, Zurich, Switzerland

R. Manka
Institute for Biomedical Engineering, University and ETH Zurich, Zurich, Switzerland

N. Cesarovic
Department of Surgical Research, University Hospital Zurich, Zurich, Switzerland

Several new transcatheter techniques have been introduced for treating MR in high risk surgical candidates. The currently most popular device is the MitraClip^{TM} that produces a double orifice by clipping the free edges of the mitral valve together [4]. Other devices are placed through percutaneous intervention into the coronary sinus with the aim to reduce the size of the posterior annulus [5, 6]. Further devices use techniques directly addressing the annulus either mechanically or using energy sources to shrink the annular tissue. The Mitralign^{TM} device uses a cinching technique at the mitral valve annulus for reducing its size. The QuamtumCor^{TM} device reduces the size of the posterior mitral annulus with radiofrequency ablation [7]. Irrespective of the device used, precise planning of such minimally invasive procedures is essential. This planning mainly includes estimations of the required device size for the individual patient before implantation.

Recently, the Cardioband^{TM} (ValtechCardio, Or Yehuda, Israel) direct annuloplasty system was introduced to closely replicate surgical implant of a posterior annuloplasty Dacron^{TM} band, with a transfemoral percutaneous approach [8]. Multidetector computed tomography (CT) has been used as an imaging modality for pre-procedural sizing of the device and planning of the Cardioband^{TM} implantation procedure. Herein we report our initial experience in the animal model that has been used for the preclinical evaluation of the device prior to human clinical trials.

Materials and methods

All animals received human care in compliance with the Swiss Animal Protection Law (TSchG) and the Swiss Animal Protection Act (TSchV). The study protocol was approved by the local Committee for Experimental Animal Research (Kantonales Veterinäramt des Kantons Zürich, permission number 161/2012).

Seven domestic pigs with a mean weight of 99.8 ± 6.9 kg (range 90–112 kg) underwent procedure planning and Cardioband^{TM} implantation. CT was performed in all animals pre- and postoperatively. General anesthesia was induced with Propofol and maintained with Propofol and Isofluran. Amiodarone (150–300 mg) was administered preoperatively to avoid arrhythmias during the procedure.

After the postoperative CT scan all animals were sacrificed and the hearts were explanted. The left ventricle's anterior wall was split from the middle of the anterior mitral leaflet to the apex. The correct positioning of the Cardioband^{TM} was verified and the length was measured at the expanded heart.

CT imaging protocol and data reconstruction

Under general anesthesia, animals were scanned twice—immediately before and after Cardioband^{TM} implantation—with a second-generation 128-section dual-source CT machine (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany) equipped with an integrated circuit detector (Stellar, Siemens Healthcare, Forchheim, Germany) [9]. The data acquisition was synchronized with the electrocardiogram (ECG) of the animals using retrospective ECG-gating, and with the following scan parameters: detector collimation $2 \times 0.6 \times 64$, slice acquisition $2 \times 0.6 \times 128$ by means of a z-flying focal spot, gantry rotation time 0.28 s, tube current–time product 380 mAs/rotation, and tube voltage 120 kVp.

80 Eighty ml iopromide (Ultravist$^{®}$ 370, Bayer Healthcare, Berlin, Germany) was used as contrast agent for the CT scans.

All CT data was reconstructed using a slice thickness of 0.6 mm and increment of 0.4 mm using sinogram-affirmed iterative reconstructions (SAFIRE) at a strength level of 3 [10]. The reconstruction field-of-view (FoV) was set to 200 mm with a pixel matrix of 512×512. Images were reconstructed in 10 % steps of the RR-interval.

Definition of the mitral annulus and CT data analysis

The mitral annulus is a fibrous cord that marks the hingeline of the 2 mitral valve leaflets. The anterior border of the mitral annulus is related to the aortic valve and the right and left fibrous trigones. In the area of aortic-mitral fibrous continuity, the distal margin of the left atrial myocardium over the leaflet defines the hingeline of the anterior mitral annulus. The area opposite of the fibrous continuity corresponds to the posterior mitral annulus [11].

The following measurements in systole (30 % of the RR-interval) and in diastole (70 % of the RR-interval) were performed using the multiplanar reformation software tool installed on the scanner workstation as described in [12]:

- After reformation in a 2D short-axis a slice was chosen where the anterolateral and posteromedial commissures could be identified. The posterior circumferential distance of the commissures was defined as the posterior mitral annular circumference and was measured free-hand (Fig. 1a),
- Shortest distance from the posterior annular circumference to the circumflex artery (CX) was measured after following the CX in its entire length (Fig. 1b),

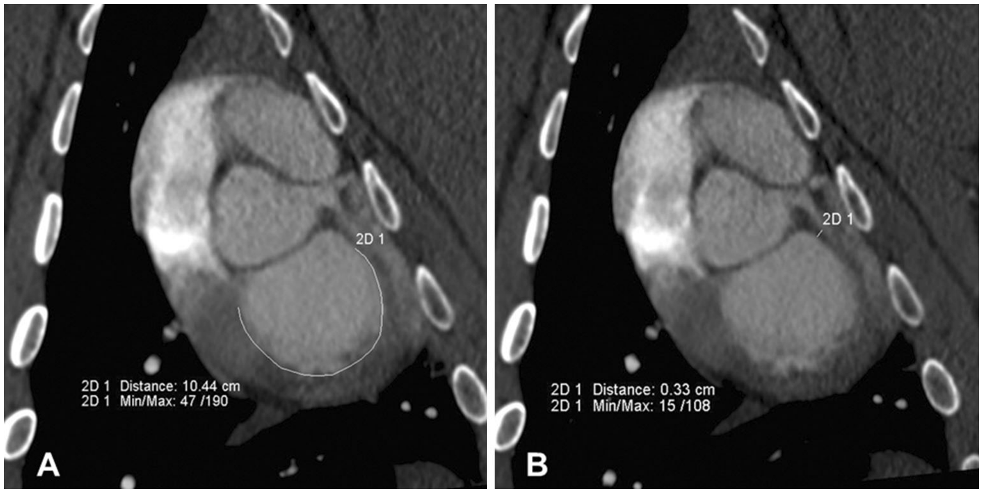

Fig. 1 CT short-axis reformations parallel to the mitral annulus showing the measurements of the **a** posterior mitral annular circumference and the **b** shortest distance of the posterior mitral annulus to the circumflex artery

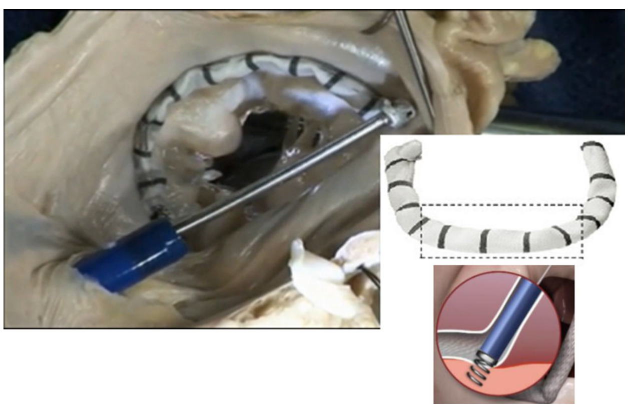

Fig. 2 Schematic representation of the Cardioband™ implantation. The *large image* shows the Cardioband™ implanted in a cadaver atrium. The *inlay picture* shows the Cardioband™ and a schematic of the anchors used to fix the device at the mitral valve annulus

- Shortest distance from the posterior annular circumference to the coronary sinus was measured after following the coronary sinus in its entire length,
- Device length by measuring free-hand the circumferential length along the device from the first anchor to the last anchor in a 2D short-axis reformation, and
- Shortest distance of the closest anchor to the CX.

The Cardioband™ device

The Cardioband™ (Valtech Cardio, Or Yehuda, Israel) consists of a delivery system made for transvenous access and a Dacron band intended to be anchored sutureless along the posterior mitral annulus from commissure to commissure in the beating heart. Iliac artery sizing is not mandatory prior to the procedure, because access to the mitral valve is gained through transseptal puncture from the right atrium which is approached from the femoral vein. Cardioband™ is fixated along the annulus using a series of stainless steel anchors delivered through the implant into the native annular tissue. After implantation, the band can be contracted or expanded with an adjustment tool under echocardiographic guidance (Fig. 2). The adjustment induces a reduction of the distance from commissure to commissure and also of the anterior–posterior diameter, and with that also increases the length of coaptation of the anterior and the posterior mitral valve leaflet.

Table 1 Available Cardioband™ sizes according to the measurements of the posterior mitral annular circumference commissure to commissure distance in mm

Length in mm	Cardioband™ size
73–80	A
81–88	B
89–96	C
97–104	D
105–112	E
113–120	F

The Cardioband™ is available in different lengths from 73 to 120 mm. The necessary size has to be chosen before the implantation and depends on the length of the posterior mitral valve annulus from commissure to commissure. The planning algorithm for the CT measurements is described below. The Cardioband™ lengths according to the measurements of the posterior mitral annular circumference commissure to commissure distance is provided in Table 1.

Implantation procedure

After preoperative CT, the animals were kept in general anesthesia and brought to the animal hybrid operating room. All implantations were performed in a state-of-the-art hybrid operating theater (Philips monoplane AlluraXper FD20C) with support of angiography and intracardiac echocardiography (ICE).

Access was gained through a right-sided, muscle sparing thoracotomy in the 4th and 5th intercostal space. Access to the right atrium was gained through a 10 mm Dacron^{TM} prosthesis, sutured to the lower part of the right atrium close to the inferior vena cava (IVC) with an angulation of around 45° meant as a neo-IVC. This step was undertaken because the angulation between the natural IVC and the mitral annular plane is more acute in pigs compared to humans. A large port-like construct was placed into the end of the prosthesis as access for the catheters and devices. A 10Fr sheath was placed in the apex of the heart, a 10Fr sheath was placed in the femoral artery as access for two ICE catheters (Acunav, Siemens Healthcare, Forchheim, Germany) that were used for guiding the implantation.

The first step of the procedure is transseptal puncture to gain access to the left atrium above the mitral valve. The Cardioband^{TM} delivery system (transseptal steerable sheath and implant delivery system) was placed into the left atrium above the mitral valve over an Amplatz Superstiff (Boston Scientific, Natick, MA, USA) guide wire. Anchors were loaded through the delivery system individually and advanced into the anchor channel through the implant. The first anchor was placed in the anterolateral commissure. Placement of further anchors was then performed in a counter-clockwise direction, until reaching the posteromedial commissure. Every intended anchoring position was confirmed by ICE and angiography. After complete implantation of the Cardioband^{TM}, it was released from the delivery system. Using a specialized catheter, the size of the Cardioband^{TM} could be reduced temporarily to proof functionality of the system, and therefore restored to its initial size. The implant delivery system would be then disconnected and the neo-IVC was ligated close to the atrial anastomosis. The thoracotomy was closed and the animals were brought to the CT again to visualize and to measure the length of the Cardioband^{TM}. After the second CT, the animals were euthanazied and the heart explanted to visually verify correct or incorrect placement of the anchors and to verify the correct length of the Cardioband^{TM} chosen before the implantation.

Results

Transseptal puncture and implantation of the first anchor of the Cardioband^{TM} could be performed in all animals. In all animals, the implantation of the whole device including retrieval of the delivery device could be successfully performed.

After sacrificing the animals, hearts were explanted. Measurements of the length of the Cardioband^{TM} could be successfully performed on postoperative CT in all animals. Gross examination found the Cardioband^{TM} adequately implanted in all animals, with no anchor dehiscence and no surrounding structure damage (including no circumflex artery lesions). In all animals the Cardioband^{TM} was implanted exactly from commissure to commissure confirming accuracy of the preoperative performed CT measurements.

Qualitative CT image analysis

The Cardioband^{TM} device did not result in a metal artifact-related degradation of image quality in any of the animals. Both the implant and the surrounding structures could be visualized on postinterventional CT with high quality. The single anchors are clearly visualized as well as the adjustment mechanism close to the first anchor (Fig. 3).

Every single anchor can be clearly identified with a screw placed in the mitral valve annulus. Close to the first anchor at the anterolateral commissure, the adjustment coil is located. The unharmed circumflex artery could be visualized clearly to exclude accidental injury to the vessel and resulting bleeding or ischemia. The Cardioband^{TM} itself was not visualized by CT.

In-vivo and ex vivo measurements

The results from in vivo and ex vivo measurements are summarized in Table 2.

Before implantation, the mitral valve circumference and the posterior mitral annulus length was 9.9 $\pm$ 0.4 cm (range 9.4–10.4 cm) during diastole and 8.94 $\pm$ 0.3 cm (range 8.5–9.4 cm) during systole. After implantation, the mean Cardioband length measured in MDCT was 8.77 $\pm$ 0.6 cm during diastole and 8.59 $\pm$ 0.4 cm during systole. Direct measurements after explantation revealed an average length of the implant of 9.87 $\pm$ 0.7 mm (Fig. 4).

The distance from the posterior mitral annulus to the CX varied among the animals, with a median distance of 3.3 $\pm$ 0.8 mm (range 3–6 mm) in diastole and 3.9 $\pm$ 1.2 mm during systole (range 1–3 mm) (see Fig. 1b).

The distance from the posterior mitral annulus to the coronary sinus varied among the animals, with a median distance of 6.4 $\pm$ 1.3 mm (range 4–8 mm) in diastole and of 7.7 $\pm$ 1.1 mm during systole (range 6–9 mm).

After implantation of the Cardioband^{TM}, the closest distance from the closest anchor to the CX was 2.1 $\pm$ 0.7 mm (range 1–3 mm) in diastole and 1.6 $\pm$ 0.5 mm (range 1–2 mm) in systole (see Fig. 3).

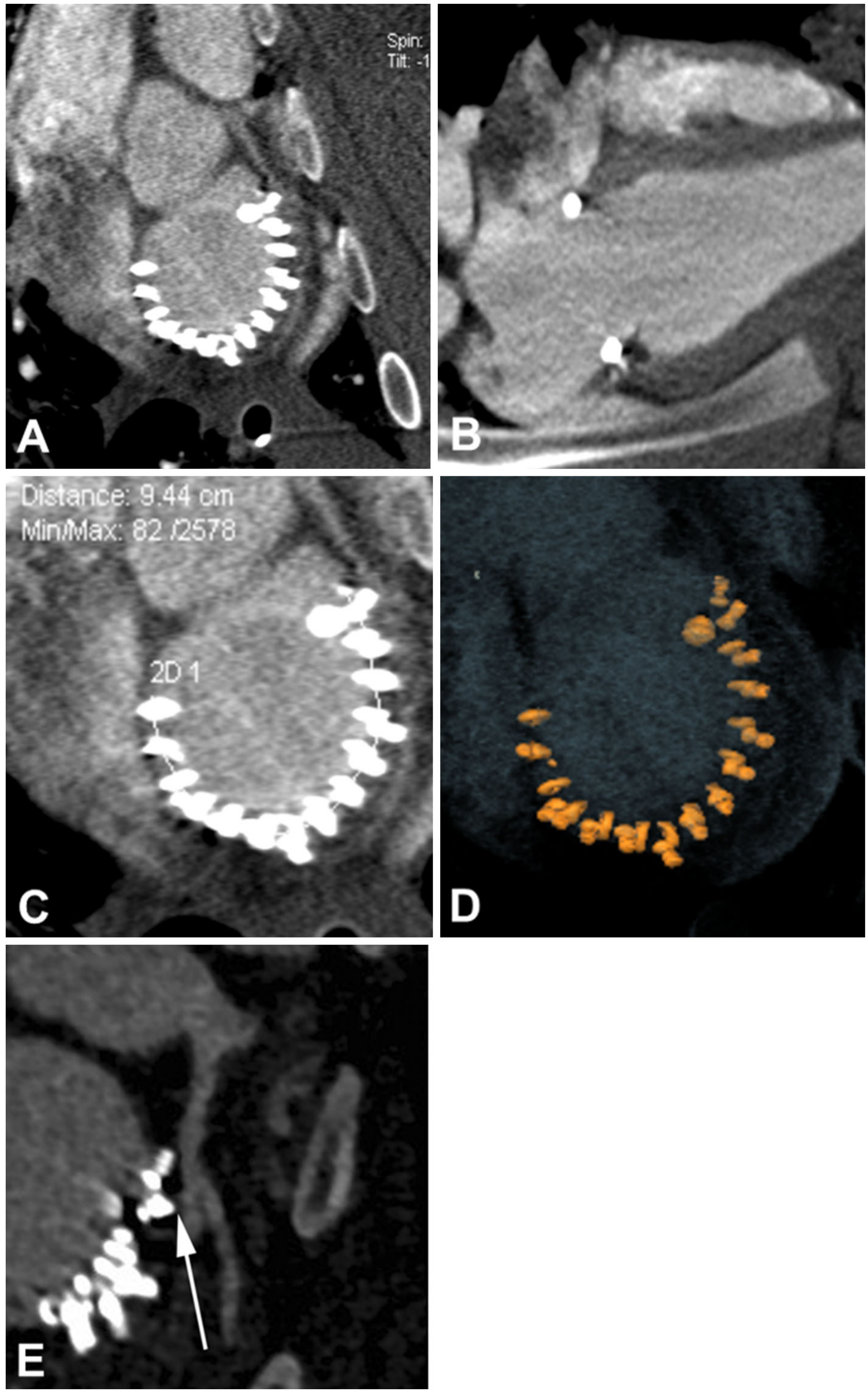

Fig. 3 CT reformations after Cardioband^{TM} implantation **a** in the short-axis and **b** in the long axis of the left ventricle. **c** Measurements of the device length after implantation and **d** 3D volume rendered image of the implant. Zoomed maximum intensity image **e** illustrates the close spatial relationship of the anchors of the device to the CX (*arrow*)

Discussion

To the best of our knowledge, this study is the first to describe the results from pre- and postoperative CT evaluation of a direct annuloplasty device. We provide measurements of the posterior mitral annulus with CT pre- and postoperatively and after intervention in explanted hearts in an animal study during preclinical evaluation of the Cardioband^{TM} system, a direct annuloplasty device replicating a surgical posterior annuloplasty band procedure.

Surgical MVR is the gold standard therapy for MR [1, 2]. Since few years, new concepts and devices are developed for off-pump interventions to avoid the need of cardiopulmonary bypass and cardioplegia. Former devices

Table 2 Measurement results for the CT and the direct measurement of the CardioBand™ (diastole/systole)

	Weight (kg)	Posterior annular length CT pre (cm) (diastole/ systole)	Cardioband length CT post (cm) (diastole/ systole)	Cardioband length Explant (cm)	Shortest distance of mitral annulus to circumflex artery (mm) (diastole/ systole)	Shortest distance of the closest anchor to the circumflex artery (mm) (diastole/systole)	Shortest distance of mitral annulus to coronary sinus/great cardiac vein (mm) (diastole/systole)
Animal 1	112	10.4/9.4	9.4/9.2	10.5	3/3	1/2	4/6
Animal 2	99.5	9.4/8.8	8.4/8.2	–	3/3	2/2	6/7
Animal 3	103	9.8/9.0	8.9/8.7	9	3/3	3/2	7/9
Animal 4	90	9.9/9.0	8.3/8.5	9.7	5/6	3/1	8/9
Animal 5	95	9.8/8.5	8.1/8.5	9.7	3/4	2/2	7/7
Animal 6	97.5	9.7/8.9	8.5/8.2	9.5	3/3	2/1	6/8
Animal 7	101.5	10.3/9.0	8.9/8.8	10.8	4/5	2/1	7/8

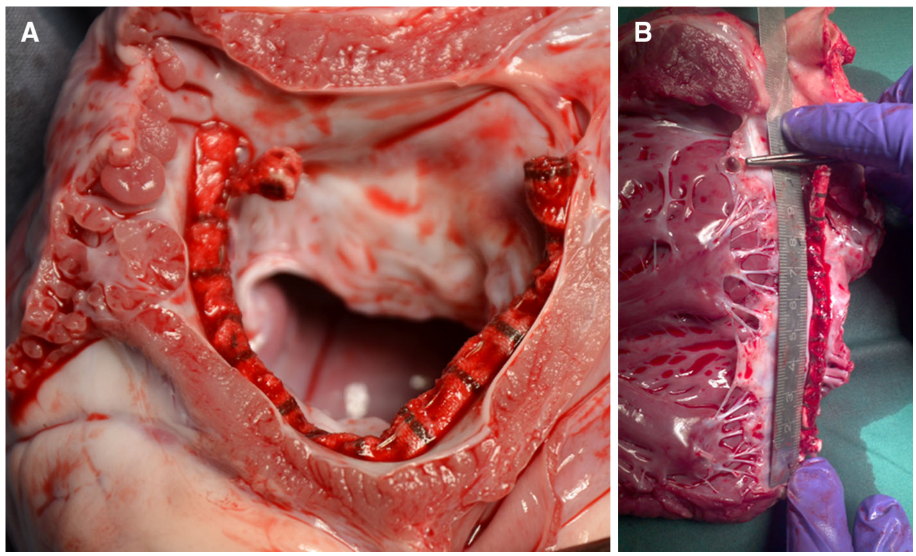

Fig. 4 Explanted pig heart after removal of the left atrium. **a** The Cardioband™ is anchored in the posterior mitral annulus from commissure to commissure along the posterior leaflet. **b** Outspread mitral annulus for manual measurement of the length of the device

focused on the CS. The MONARC and the CARILLON device are placed in the CS via a catheter and are intended to improve leaflet coaptation in secondary mitral valve regurgitation [5, 6]. The concept of these devices was shown to be feasible, but clinical results are not yet convincing. Main issues are the variability of the coronary sinus anatomy and the potential for compressing the circumflex artery. More recently, direct annuloplasty has gained growing interest, as the ideal approach for percutaneous mitral valve annuloplasty. The Cardioband™ device is intended to be anchored directly to the mitral valve posterior annulus from commissure to commissure. Promising results are available from an animal trial with direct atrial approach [8]. An important issue of such procedures is precise planning and pre-procedural choice of the correct implant size. Standard modality for mitral valve imaging pre-, post- and intraoperatively actually is transesophageal echocardiography (TEE) [2, 13, 14]. One major concern about TEE is operator dependency and reproducibility of echocardiographic results [15]. Besides TEE, CT has been described for assessment of the mitral valve anatomy for patients with normal renal function that can be harmed with contrast medium. Delgado and colleagues assessed mitral valve anatomy and geometry with 64-slice CT in a cohort of 151 consecutive patients [16]. Besides others, they measured mitral valve area, diameter from commissure to commissure and anteroposterior diameter. Patients with and without secondary MR were compared, and differences in mitral valve geometry were demonstrated. However, no systematic surgical assessment of the patients was available to confirm their CT measurements.

In a study performed by our group, we assessed the three-dimensional shape of the mitral valve in order to produce patient-specific annuloplasty rings in an animal experiment [17]. In this study, CT was used to produce an exact model of the mitral valve annulus. In a rapid prototyping procedure, rings were produced from these models and implanted in 6 healthy pigs. It could be observed, that the shape of the rings matched almost perfectly to the annular circumference. From this data, we concluded that assessment of the mitral annulus with CT is feasible and offers an exact visualization of the structures of interest. In a recent study by Wang and colleagues [18], CT was used as basis for finite element modeling of the mitral valve. Only one patient was identified as eligible out of a database for the study due to sufficient image quality. From these images a model of the whole mitral valve within systole and diastole could be constructed. This confirms the role and the importance of use and improvement of CT imaging in mitral valve disease. In our study we compared the annular dimension in systole and diastole, too. We found the posterior annulus length to be decreased around 10 % during systole. This corresponds to in vivo findings in humans [19]. We could not find in the literature such measurements in animals.

In this study, CT reliably predicted posterior annular size in all animals undergoing the procedure. Compared to baseline, annular size was slightly reduced in the follow-up CT, especially compared to the diastolic measurement, due to some residual cinching after Cardioband™ implantation. The Cardioband™ was intentionally disconnected with minimal amount of cinching in this study to focus on CT sizing performance. However, we must acknowledge the study limitation that our animal population was rather homogenous in size, and our results suggest that a 9.5–10 cm ring could have been used in all animals.

In addition, CT allowed for an evaluation of the shortest distance from the posterior mitral annulus to the CX and to the coronary sinus prior to intervention, and allowed for a depiction of the spatial relationship and distance of the closest anchor to the CX and coronary sinus after Cardioband™ implantation. The distance from the anchor to the CX varied between 1 and 3 mm in this study. No injuries or impingements of the CX were found in gross examination. Nevertheless, this remains a potential complication of the procedure. Therefore, we consider it important to obtain precise imaging of these structures prior to implantation to be aware of the exact close anatomical proximity which might increase the risk of these complications. Together these findings support the use of CT as an adjunct to TEE for procedure planning and for post-interventional control in mitral valve procedures for ongoing and future clinical trials.

Currently, Cardioband™ is under clinical evaluation in a feasibility and safety human trial. Patient selection and device sizing is strongly supported by CT derived imaging. CT is used to size the annulus, in a similar fashion to what described here, and to guide device size selection. In addition, CT offers invaluable information relative to anatomy of the annulus, relationship with the circumflex artery, and presence and quantification of annular or leaflet calcification, which would be a contraindication for any annuloplasty procedure.

Another fact underlining the importance of CT as planning tool is that in contrast to mitral valve interventions, for transcatheter aortic valve implantation (TAVI) procedures, computed tomography already has become the standard imaging modality to plan the procedure [20] due to its versatility, 3D nature and low interobserver variability.

Besides transcatheter MVR, MV replacement will be an important alternative therapie for high risk patients with MV disease in the future. Several prosthesis are under preclinical evaluation or have already witnessed their first-in-human implantation [21]. For planning of these procedures, as for TAVI procedures, CT will be a very important imaging tool.

In conclusion, preoperative measured length of the distance between postero-medial and antero-lateral commissure adequately predicted the necessary length of the Cardioband™ to be implanted as shown by the gross examination after explantation of the hearts. Postoperative CT showed the intentionally cinched and released Cardioband™ a little shorter then measured after explantation. This might be explained by the "floppy" character of the heart after explantation: The Cardioband™ then expands to its initial length but not in the beating heart.

In conclusion, transvenous implantation of a Cardioband™ at the posterior mitral annulus is feasible in an acute animal model. CT visualization and measurement of the mitral valve annulus dimensions can become the imaging method of choice for procedure planning before implantation of a Cardioband™ or other transcatheter devices that are already available or will be available in the future.

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Conflict of interest Volkmar Falk and Francesco Maisano are consultants for Valtech Cardio.

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